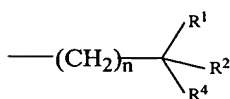


1



wherein R<sup>a</sup> is H or a

group;



is an aryl or heteroaryl group;

X is H, halogen, -OH, -CN, -C≡C-R<sup>3a</sup>, a -C<sub>1</sub>-C<sub>4</sub> alkyl group optionally substituted with from one to three halogen atoms, or a -O(C<sub>1</sub>-C<sub>4</sub> alkyl) group optionally substituted with from one to three halogen atoms;

Q is H, halogen, a C<sub>1</sub>-C<sub>6</sub> alkyl, -OH, -CN, -OCH<sub>3</sub>, -NH<sub>2</sub>, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)NH<sub>2</sub>, -C(=O)NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -NHC(=O)R<sup>15</sup>, -NHS(=O)<sub>2</sub>R<sup>15</sup>, a 5- to 7-membered carbocyclic or heterocyclic group, or forms a 5- to 7-membered phenyl-fused or heteroaryl-fused carbocyclic or heterocyclic group with an adjacent atom on the phenyl or heteroaryl group to which it is attached, said phenyl-fused or heteroaryl-fused carbocyclic or heterocyclic group optionally containing at least one unsaturated bond, said heterocyclic group or said phenyl-fused or heteroaryl-fused heterocyclic group containing at least one heteroatom selected from nitrogen, oxygen and sulfur, said carbocyclic or heterocyclic group or said phenyl- or heteroaryl-fused carbocyclic or heterocyclic group being optionally substituted with at least one substituent selected from H, halogen, -OH, =O, -C≡C-R<sup>3a</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl, -O(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, or -(CH<sub>2</sub>)<sub>n</sub>-aryl, wherein said C<sub>1</sub>-C<sub>6</sub> alkyl, -O(C<sub>1</sub>-C<sub>6</sub>)alkyl, or C<sub>3</sub>-C<sub>6</sub> cycloalkyl groups optionally may be substituted by one or more halogen atoms and said aryl portion of said -(CH<sub>2</sub>)<sub>n</sub>-aryl is optionally substituted by one or more substituents selected from H, halogen, C<sub>1</sub>-C<sub>4</sub> alkyl and -O(C<sub>1</sub>-C<sub>4</sub>)alkyl, said C<sub>1</sub>-C<sub>4</sub> alkyl and -O(C<sub>1</sub>-C<sub>4</sub>)alkyl groups being optionally substituted by one

or more halogen atoms,  $-N(R^{4a})(R^{5a})$ ,  $-N(R^{4b})S(O)_mR^{6a}$ ,  $-N(R^{4c})C(O)R^{7a}$  or  $-N(R^{4d})C(O)OR^{7b}$  groups;

$R^{3a}$ ,  $R^{4a}$ ,  $R^{4b}$ ,  $R^{4c}$ ,  $R^{4d}$  and  $R^{5a}$  are independently H or C<sub>1</sub>-C<sub>6</sub> alkyl which may be optionally substituted with one or more halogen groups, or  $R^{4a}$  and  $R^{5a}$ , together with the nitrogen atom to which they are bound, form a 4- to 7-membered heterocyclic group which may be unsubstituted or substituted with one or more substituents selected from C<sub>1</sub>-C<sub>4</sub> alkyl, -O(C<sub>1</sub>-C<sub>4</sub>)alkyl, -OH, =O, -NR<sup>16a</sup>R<sup>16b</sup>, halogen or -C≡C-R<sup>3a</sup>;

$R^{6a}$  is a C<sub>1</sub>-C<sub>6</sub> alkyl, an aryl or a heteroaryl group wherein said alkyl, aryl or heteroaryl group is unsubstituted or substituted with one or more substituents selected from halogen, C<sub>1</sub>-C<sub>4</sub> alkyl, -OH, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), -(C<sub>1</sub>-C<sub>4</sub> alkyl)-O-(C<sub>1</sub>-C<sub>4</sub> alkyl) or -(CH<sub>2</sub>)<sub>n</sub>-NR<sup>21</sup>R<sup>22</sup>;

$R^{7a}$  and  $R^{7b}$  are independently selected from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl (wherein each of said C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl may independently be unsubstituted or substituted with halogen or C<sub>1</sub>-C<sub>4</sub> alkyl substituents), or  $R^{7a}$  is H;

$R^1$  and  $R^2$  are independently H, a C<sub>1</sub>-C<sub>6</sub> alkyl, -(CH<sub>2</sub>)<sub>j</sub>-aryl, -(CH<sub>2</sub>)<sub>j</sub>-heteroaryl, wherein said alkyl, -(CH<sub>2</sub>)<sub>j</sub>-aryl or -(CH<sub>2</sub>)<sub>j</sub>-heteroaryl group is optionally substituted with one or more R<sup>16</sup> groups, or with the carbon to which  $R^1$  and  $R^2$  are attached,  $R^1$  and  $R^2$  form a C<sub>3</sub>-C<sub>7</sub> carbocyclic or 4- to 7-membered heterocyclic group, wherein said heterocyclic group comprises from one to three heteroatoms selected from the group consisting of O, S and N and said carbocyclic or heterocyclic group optionally contains a -C(=O) group or optionally contains one or more double bonds and is optionally fused to or substituted with a C<sub>6</sub>-C<sub>14</sub> aryl or a 5- to 14-membered heteroaryl group, wherein said C<sub>3</sub>-C<sub>7</sub> carbocyclic or 4- to 7-membered heterocyclic group formed by  $R^1$  and  $R^2$  may optionally be substituted with from one to three R<sup>16</sup> groups, and said optionally fused or substituted aryl or heteroaryl group may each optionally independently be substituted with from one to six R<sup>16</sup> groups;

each R<sup>16</sup> is independently selected from R<sup>17</sup>, H, halogen, -OR<sup>17</sup>, -NO<sub>2</sub>, -CN, -C<sub>1</sub>-C<sub>6</sub> alkyl, -C<sub>3</sub>-C<sub>6</sub> cycloalkyl, -C(R<sup>4</sup>)R<sup>16a</sup>R<sup>16b</sup>, aryl optionally substituted with from 1 to 3 R<sup>4</sup> groups, -(CH<sub>2</sub>)<sub>v</sub>NR<sup>17</sup>R<sup>18</sup>, -NR<sup>17</sup>C(=O)R<sup>18</sup>, -C(=O)NR<sup>17</sup>R<sup>18</sup>, -OC(=O)R<sup>17</sup>, -C(=O)OR<sup>17</sup>, -C(=O)R<sup>17</sup>, -NR<sup>17</sup>C(=O)OR<sup>18</sup>, -NR<sup>17</sup>C(=O)N R<sup>18</sup>R<sup>19</sup>, -NR<sup>17</sup>S(=O)<sub>2</sub>R<sup>18</sup>, -NR<sup>17</sup>S(=O)<sub>2</sub>NR<sup>18</sup>R<sup>19</sup>, and -S(=O)<sub>2</sub>R<sup>17</sup>;

$R^3$  is H, F, Cl, -OH, -C<sub>1</sub>-C<sub>4</sub> alkyl, -C≡N, -NR<sup>17</sup>C(=O)R<sup>18</sup>, -C(=O)NR<sup>17</sup>R<sup>18</sup>, -O(C<sub>1</sub>-C<sub>4</sub>)alkyl, -(CH<sub>2</sub>)<sub>n</sub>OH, -(CH<sub>2</sub>)<sub>n</sub>-C≡N, -(CH<sub>2</sub>)<sub>n</sub>-NR<sup>17</sup>C(=O)R<sup>18</sup>, -(CH<sub>2</sub>)<sub>n</sub>-C(=O)NR<sup>17</sup>R<sup>18</sup>, -(CH<sub>2</sub>)<sub>n</sub>-O(C<sub>1</sub>-C<sub>4</sub>)alkyl, or -(CH<sub>2</sub>)<sub>n</sub>-NR<sup>16a</sup>R<sup>16b</sup>;

$R^4$  is absent or is H, -C<sub>1</sub>-C<sub>4</sub> alkyl, which optionally contains one or two unsaturated bonds, -OH, -O(C<sub>1</sub>-C<sub>4</sub>)alkyl, -(C<sub>1</sub>-C<sub>4</sub>)alkylOH, -(CH<sub>2</sub>)<sub>n</sub>-NR<sup>16a</sup>R<sup>16b</sup>, -(CH<sub>2</sub>)<sub>n</sub>-NHC(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -(CH<sub>2</sub>)<sub>n</sub>-NO<sub>2</sub>, -(CH<sub>2</sub>)<sub>n</sub>-C≡N, -(CH<sub>2</sub>)<sub>n</sub>-C(=O)NH<sub>2</sub>, -(CH<sub>2</sub>)<sub>n</sub>-C(=O)NR<sup>16a</sup>R<sup>16b</sup>;

$R^5$  and  $R^8$  are independently selected from H, Cl, F, -OH, C<sub>1</sub>-C<sub>4</sub> alkyl, -O(C<sub>1</sub>-C<sub>4</sub>)alkyl, -C(=O)R<sup>20</sup>, -(C<sub>1</sub>-C<sub>4</sub> alkyl)-OR<sup>20</sup>, -C(=O)OR<sup>20</sup>, -OC(=O)R<sup>20</sup>, -S(O)<sub>m</sub>R<sup>20</sup> and -NH<sub>2</sub>SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub>)alkyl;

$R^6, R^7, R^9, R^{10}, R^{11}, R^{12}, R^{13}$  and  $R^{14}$  are each independently selected from H, F, Cl, -OH,  $-(C_1-C_4)\text{alkyl}$  and  $-O(C_1-C_4)\text{alkyl}$ ;

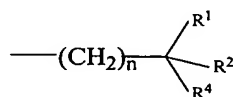
$R^{15}, R^{17}, R^{18}$  and  $R^{19}$  are independently H,  $-C_1-C_4$  alkyl,  $-(C_2-C_4 \text{ alkyl})-O-(C_1-C_4 \text{ alkyl})$ ,  $-(CH_2)_v-NR^{21}R^{22}$ , or a 4- to 7-membered heterocyclic group optionally substituted with a  $-C_1-C_4$  alkyl;

each  $R^{16a}$  and  $R^{16b}$  is independently selected from H and  $C_1-C_4$  alkyl; or, independently in each instance of  $-C(R^4)R^{16a}R^{16b}$ ,  $R^{16a}$  and  $R^{16b}$  connect to form a  $C_3-C_7$  carbocyclic ring;

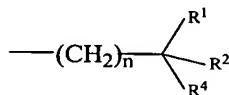
$R^{20}$  is a  $C_1-C_4$  alkyl group, a  $C_3-C_7$  carbocyclic or a 4- to 7-membered heterocyclic group comprising from one to three heteroatoms selected from the group consisting of O, S and N, wherein said carbocyclic and heterocyclic groups are optionally independently substituted with from one to three  $R^{16}$  groups, optionally independently contain one or more double bonds, and are optionally fused to a  $C_6-C_{14}$  aryl or a  $C_5-C_{14}$  heteroaryl group comprising from one to three heteroatoms selected from the group consisting of O, S and N, and wherein said optionally fused aryl or heteroaryl groups can each optionally independently be substituted with from one to six  $R^{16}$  groups;

$R^{21}$  and  $R^{22}$  are each independently H or  $C_1-C_6$  alkyl; or, independently in each instance of  $-NR^{21}R^{22}$ ,  $R^{21}$  and  $R^{22}$  connect to form a 4- to 7-membered heterocyclic ring comprising from one to three hetero atoms selected from O, S, and N;

$j$  is in each instance independently an integer from 0 to 5;  
 $m$  is in each instance independently an integer from 0 to 2;  
 $n$  is in each instance independently an integer from 0 to 5;  
 $v$  is in each instance independently an integer from 0 to 5;  
 or a pharmaceutically acceptable salt thereof;  
 with the provisos that

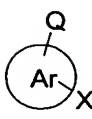


a) when  $R^a$  is and  $n$  is 0, and when the carbon to which  $R^1, R^2$  and  $R^4$  are bound is  $sp^3$  hybridized (i.e., "saturated"), then none of  $R^1, R^2$  and  $R^4$  can be a heteroatom or contain a heteroatom which is directly linked to the carbon of said



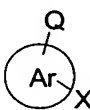
group;

b)  $R^{15}$  cannot be H when part of a  $-NHS(=O)_2R^{15}$  group,  $R^{17}$  cannot be H when part of a  $-S(=O)_2R^{17}$  group and  $R^{18}$  cannot be H when part of a  $-NR^{17}S(=O)_2R^{18}$  group;

c) when  $R^3$  is  $OCH_3$  or  $OH$ ,  cannot be 3-hydroxyphenyl or 3-methoxyphenyl;

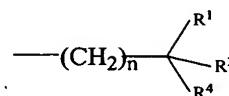
d) when  is a phenyl group, then Q and X are not both H;


e) when  $-(CH_2)_v-$  is connected to N, O, or S, then v cannot be 1; and

f)  cannot be 4-(6-amino-pyridin-2-yl)-phenyl.

5 2. A compound according to claim 1 wherein  $R^a$  is a


group and wherein  is a phenyl group.

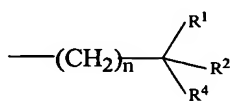


3. A compound according to claim 2 wherein  is a phenyl group and Q is substituted at a meta position on said phenyl group and is selected from  $-C(=O)NH_2$ ,  $-OH$  and  $-NHSO_2R^{15}$ .

10 4. A compound according to claim 2 wherein X is H, F or  $C \equiv N$ .

5. A compound according to any of claim 2, wherein  $R^3$  is H, OH, Cl, methyl, ethyl, isopropyl, OMe, OEt, O-*i*Pr, O-allyl or O-*n*-Pr.

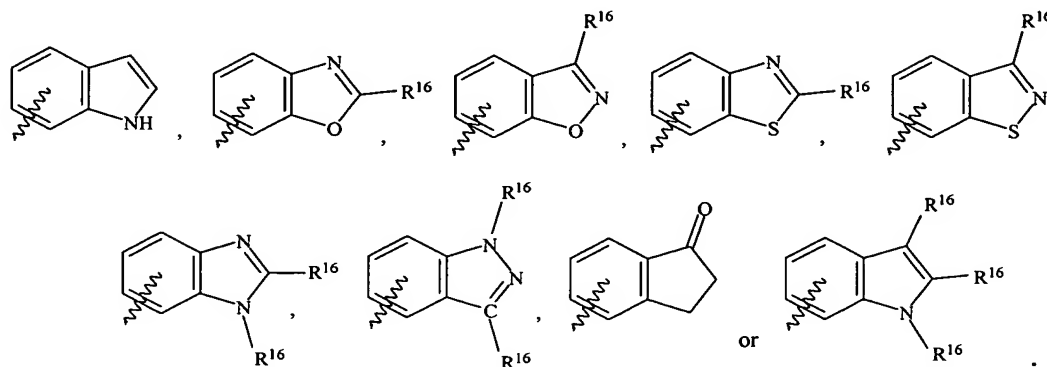
6. A compound according to claim 1, wherein  is a phenyl group; Q is substituted at a meta position on said phenyl group and is selected from  $-C(=O)NH_2$ ,  $-OH$  and

15  $-NHSO_2R^{15}$ ;  $R^a$  is a  group; and  $R^1$  and  $R^2$  taken together with the carbon to which they are attached form a cyclobutane, cyclopentane, cyclohexane, indane-2-yl or 1,2,3,4-tetrahydronaphth-2-yl which may be unsubstituted or substituted with  $R^{16}$  groups; and wherein  $R^4$  is H, OH,  $-NH(=O)-CH_3$ ,  $-C(=O)NH_2$ ,  $-CH_2OH$  or  $-OCH_3$ .

7. A compound according to claim 2, wherein n is 1, 2 or 3.

20 8. A compound according to claim 2  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$ ,  $R^{13}$  and  $R^{14}$  are each H.

9. A compound according to claim 1 wherein Q forms a phenyl-fused heterocyclic group with the adjacent phenyl group, wherein said Q group and said phenyl group form a group according to the chemical structure:



- 5 10. A compound according to claim 1 selected from
- 3-(3-Cyclopropylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenol;
- 3-(3-Ethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-(3-Cyclopropylmethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-[3-(3-Cyclohexyl-propyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenol;
- 10 3-[8-Methoxy-3-(3-methyl-butyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 3-(8-Methoxy-3-pentyl-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-[8-Methoxy-3-(1H-pyrrol-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 3-(3-Hexyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-[3-(2-Ethyl-butyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 15 2-[8-(3-Hydroxy-phenyl)-3-aza-bicyclo[3.2.1]oct-3-ylmethyl]-indan-2-ol;
- 3-[8-Methoxy-3-(1-methyl-1H-pyrrol-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 3-(8-Methoxy-3-thiophen-3-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-(8-Methoxy-3-thiazol-2-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 20 3-[3-(1-Hydroxy-cyclohexyl)-propyl]-8-(3-hydroxy-phenyl)-3-aza-bicyclo[3.2.1]octan-8-ol;
- N-[3-(3-Cyclopropylmethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- 3-(8-Methoxy-3-phenethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 25 3-(2-Hydroxy-indan-2-ylmethyl)-8-(3-hydroxy-phenyl)-3-aza-bicyclo[3.2.1]octan-8-ol;
- N-[3-(3-Isobutyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- 3-(8-Methoxy-3-octyl-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-[3-(3-(1-Hydroxy-cyclohexyl)-propyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenol;

- 3-[8-Methoxy-3-(3-phenyl-prop-2-ynyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;  
3-[8-Methoxy-3-(3-phenyl-propyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;  
2-[8-(3-Hydroxy-phenyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-3-ylmethyl]-indan-2-ol;  
N-{3-[8-Methoxy-3-(3-methyl-butyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-  
5 methanesulfonamide;  
N-[3-(8-Methoxy-3-pentyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;  
3-[3-(1H-Indol-3-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;  
3-(3-Benzofuran-2-ylmethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;  
3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-  
10 yl]-benzamide;  
N-{3-[3-(2-Ethyl-butyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-  
methanesulfonamide;  
N-[3-(3-Hexyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;  
3-(8-Methoxy-3-naphthalen-2-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;  
15 3-{3-[3-(1-Hydroxy-cyclohexyl)-propyl]-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl}-  
benzamide;  
3-(8-Methoxy-3-quinolin-3-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;  
N-[3-(8-Methoxy-3-pyridin-3-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-  
methanesulfonamide;  
20 3-[3-(4-Chloro-2-fluoro-benzyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;  
3-[8-Methoxy-3-(1-methyl-1H-indol-3-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-  
benzamide;  
3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-hydroxy-3-aza-  
bicyclo[3.2.1]oct-8-yl]-benzamide;  
25 3-[3-(2-Hydroxy-indan-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-  
benzamide;  
N-[3-(8-Methoxy-3-thiazol-2-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-  
methanesulfonamide;  
3-[8-Methoxy-3-(2-phenethyloxy-ethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;  
30 N-[3-(3-Heptyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;  
2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-pentyl-3-aza-bicyclo[3.2.1]oct-8-yl)-  
phenyl]-amide;  
2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(3-methyl-butyl)-3-aza-  
bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;  
35 N-[3-(8-Methoxy-3-phenethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-  
methanesulfonamide;

- 3-[3-(4-Hydroxy-naphthalen-1-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- N-{3-[3-(4-Fluoro-benzyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 5 3-[8-Methoxy-3-(4-pyrrolidin-1-yl-benzyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 3-[8-Methoxy-3-(3-methyl-benzo[b]thiophen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 10 3-[3-(1-Hydroxy-3-phenyl-cyclobutylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- N-{3-[3-(2-Ethyl-hexyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- N-[3-(8-Methoxy-3-octyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- 15 2-Methoxy-ethanesulfonic acid [3-(3-hexyl-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 3-(3-Biphenyl-4-ylmethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- N-{3-[3-(2-Hydroxy-indan-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 20 N-{3-[8-Methoxy-3-(4-methoxy-benzyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-pyridin-3-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 3-[8-Methoxy-3-(3-trifluoromethoxy-benzyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 25 N-{3-[3-(4-Chloro-benzyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-thiophen-3-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 2-Methoxy-ethanesulfonic acid [3-(3-cyclohexylmethyl-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 30 N-(3-{8-Hydroxy-3-[3-(1-hydroxy-cyclohexyl)-propyl]-3-aza-bicyclo[3.2.1]oct-8-yl}-phenyl)-methanesulfonamide;
- 3-[3-(9H-Fluoren-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- N-{3-[3-(1H-Indol-3-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 35 methanesulfonamide;
- N-[3-(3-Benzofuran-2-ylmethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;

- N-{3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 3-[8-Methoxy-3-(3-phenoxy-benzyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- N-{3-[8-Hydroxy-3-(2-hydroxy-indan-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 5 3-[3-(4-Dimethylamino-naphthalen-1-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-phenethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 10 N-[3-(8-Methoxy-3-naphthalen-1-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- N-[3-(8-Methoxy-3-naphthalen-2-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- N-(3-{3-[3-(1-Hydroxy-cyclohexyl)-propyl]-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl}-phenyl)-methanesulfonamide;
- 15 N-[3-(8-Methoxy-3-quinolin-4-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- N-[3-(8-Methoxy-3-quinolin-3-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- 20 N-{3-[3-(4-Chloro-2-fluoro-benzyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-octyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- N-{3-[8-Methoxy-3-(1-methyl-1H-indol-3-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 25 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(3-phenyl-prop-2-ynyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- N-{3-[8-Hydroxy-3-(2-hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 30 N-{3-[3-(2-Hydroxy-indan-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(3-phenyl-propyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 2-Methoxy-ethanesulfonic acid {3-[3-(4-chloro-benzyl)-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 35 N-{3-[3-(4-Hydroxy-naphthalen-1-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;



- 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(1H-indol-3-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- N-{3-[8-Methoxy-3-(4-pyrrolidin-1-yl-benzyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 5 N-{3-[8-Methoxy-3-(3-methyl-benzo[b]thiophen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 2-Methoxy-ethanesulfonic acid [3-(3-benzofuran-2-ylmethyl-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- N-{3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 10 2,2,2-Trifluoro-N-{3-[3-(2-hydroxy-indan-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-acetamide;
- N-[3-(3-Biphenyl-4-ylmethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- 15 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-naphthalen-2-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-naphthalen-1-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 2-Methoxy-ethanesulfonic acid (3-{8-hydroxy-3-[3-(1-hydroxy-cyclohexyl)-propyl]-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl)-amide;
- 20 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-quinolin-4-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-quinolin-3-ylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 25 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(1-methyl-1H-indol-3-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- N-{3-[8-Methoxy-3-(3-trifluoromethoxy-benzyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 2-Methoxy-ethanesulfonic acid{3-[3-(2-hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 30 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(2-hydroxy-indan-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- N-{3-[3-(9H-Fluoren-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 35 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(2-phenethyloxy-ethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;

- N-{3-[8-Methoxy-3-(3-phenoxy-benzyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- N-{3-[3-(4-Dimethylamino-naphthalen-1-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 5 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(4-hydroxy-naphthalen-1-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(4-pyrrolidin-1-yl-benzyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(3-methyl-benzo[b]thiophen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 10 2-Methoxy-ethanesulfonic acid {3-[3-(2-hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 2-Methoxy-ethanesulfonic acid {3-[3-(2-hydroxy-indan-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 15 2-Methoxy-ethanesulfonic acid [3-(3-biphenyl-4-ylmethyl-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 2-Methoxy-ethanesulfonic acid {3-[3-(2-hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 2-Methoxy-ethanesulfonic acid {3-[3-(9H-fluoren-2-ylmethyl)-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 20 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(3-phenoxy-benzyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide; and
- 2-Methoxy-ethanesulfonic acid {3-[3-(4-dimethylamino-naphthalen-1-ylmethyl)-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 25 3-(3-Cyclopropylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenol;
- 3-(3-Ethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-(3-Cyclopropylmethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-[3-(3-Cyclohexyl-propyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenol;
- 3-[8-Methoxy-3-(3-methyl-butyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 30 3-(8-Methoxy-3-pentyl-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-(3-Hexyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-[3-(2-Ethyl-butyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 2-[8-(3-Hydroxy-phenyl)-3-aza-bicyclo[3.2.1]oct-3-ylmethyl]-indan-2-ol;
- 3-[3-(1-Hydroxy-cyclohexyl)-propyl]-8-(3-hydroxy-phenyl)-3-aza-bicyclo[3.2.1]octan-8-
- 35 ol;
- N-[3-(3-Cyclopropylmethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;

- 3-(2-Hydroxy-indan-2-ylmethyl)-8-(3-hydroxy-phenyl)-3-aza-bicyclo[3.2.1]octan-8-ol;  
N-[3-(3-Isobutyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-  
methanesulfonamide;
- 5 3-(8-Methoxy-3-octyl-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;  
3-[8-Methoxy-3-(3-phenyl-propyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;  
N-{3-[8-Methoxy-3-(3-methyl-butyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-  
methanesulfonamide;  
N-[3-(8-Methoxy-3-pentyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;  
3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-  
10 yl]-benzamide;  
N-{3-[3-(2-Ethyl-butyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-  
methanesulfonamide;  
N-[3-(3-Hexyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;  
3-{3-[3-(1-Hydroxy-cyclohexyl)-propyl]-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl}-  
15 benzamide;  
3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-hydroxy-3-aza-  
bicyclo[3.2.1]oct-8-yl]-benzamide;  
3-[3-(2-Hydroxy-indan-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-  
benzamide;
- 20 3-[8-Methoxy-3-(2-phenethyloxy-ethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;  
N-[3-(3-Heptyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;  
2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-pentyl-3-aza-bicyclo[3.2.1]oct-8-yl)-  
phenyl]-amide;  
2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(3-methyl-butyl)-3-aza-  
25 bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;  
N-[3-(8-Methoxy-3-phenethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-  
methanesulfonamide;  
N-{3-[3-(4-Fluoro-benzyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-  
methanesulfonamide;
- 30 3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-methoxy-3-aza-  
bicyclo[3.2.1]oct-8-yl]-benzamide;  
3-[3-(1-Hydroxy-3-phenyl-cyclobutylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-  
benzamide;  
N-{3-[3-(2-Ethyl-hexyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-  
35 methanesulfonamide;  
N-[3-(8-Methoxy-3-octyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;

- 2-Methoxy-ethanesulfonic acid [3-(3-hexyl-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- N-{3-[3-(2-Hydroxy-indan-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 5 N-{3-[3-(4-Chloro-benzyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 2-Methoxy-ethanesulfonic acid [3-(3-cyclohexylmethyl-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- N-(3-{8-Hydroxy-3-[3-(1-hydroxy-cyclohexyl)-propyl]-3-aza-bicyclo[3.2.1]oct-8-yl}-phenyl)-methanesulfonamide;
- 10 N-{3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- N-{3-[8-Hydroxy-3-(2-hydroxy-indan-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 15 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-phenethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- N-(3-{3-[3-(1-Hydroxy-cyclohexyl)-propyl]-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl}-phenyl)-methanesulfonamide;
- 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-octyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 20 N-{3-[8-Hydroxy-3-(2-hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- N-{3-[3-(2-Hydroxy-indan-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 25 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(3-phenyl-propyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- N-{3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 2,2,2-Trifluoro-N-{3-[3-(2-hydroxy-indan-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-acetamide;
- 30 2-Methoxy-ethanesulfonic acid (3-{8-hydroxy-3-[3-(1-hydroxy-cyclohexyl)-propyl]-3-aza-bicyclo[3.2.1]oct-8-yl}-phenyl)-amide;
- 2-Methoxy-ethanesulfonic acid{3-[3-(2-hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 35 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(2-hydroxy-indan-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;

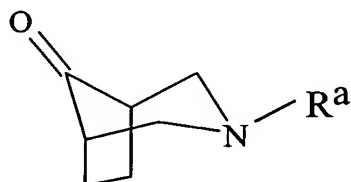
- 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(2-phenethyloxy-ethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 2-Methoxy-ethanesulfonic acid {3-[3-(2-hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 5 2-Methoxy-ethanesulfonic acid {3-[3-(2-hydroxy-indan-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 2-Methoxy-ethanesulfonic acid {3-[3-(2-hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 10 3-(3-Ethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-(3-Cyclopropylmethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-[8-Methoxy-3-(3-methyl-butyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 3-(8-Methoxy-3-pentyl-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-(3-Hexyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-[3-(2-Ethyl-butyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 15 3-(8-Methoxy-3-octyl-3-aza-bicyclo[3.2.1]oct-8-yl)-benzamide;
- 3-[8-Methoxy-3-(3-phenyl-propyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 3-{3-[3-(1-Hydroxy-cyclohexyl)-propyl]-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl}-benzamide;
- 20 benzamide;
- 3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 3-[3-(2-Hydroxy-indan-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 25 3-[8-Methoxy-3-(2-phenethyloxy-ethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 3-[3-(1-Hydroxy-3-phenyl-cyclobutylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-benzamide;
- 30 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-pentyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(3-methyl-butyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 2-Methoxy-ethanesulfonic acid [3-(3-hexyl-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 35 2-Methoxy-ethanesulfonic acid [3-(3-cyclohexylmethyl-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;

- 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-phenethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 2-Methoxy-ethanesulfonic acid [3-(8-hydroxy-3-octyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-amide;
- 5 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(3-phenyl-propyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 2-Methoxy-ethanesulfonic acid (3-[8-hydroxy-3-[3-(1-hydroxy-cyclohexyl)-propyl]-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl)-amide;
- 2-Methoxy-ethanesulfonic acid{3-[3-(2-hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 10 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(2-hydroxy-indan-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 2-Methoxy-ethanesulfonic acid {3-[8-hydroxy-3-(2-phenethyloxy-ethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 15 2-Methoxy-ethanesulfonic acid {3-[3-(2-hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 2-Methoxy-ethanesulfonic acid {3-[3-(2-hydroxy-indan-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 2-Methoxy-ethanesulfonic acid {3-[3-(2-hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-amide;
- 20 N-[3-(3-Cyclopropylmethyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- N-[3-(3-Isobutyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- 25 N-{3-[8-Methoxy-3-(3-methyl-butyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- N-[3-(8-Methoxy-3-pentyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- N-{3-[3-(2-Ethyl-butyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 30 N-[3-(3-Hexyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- N-[3-(3-Heptyl-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- N-[3-(8-Methoxy-3-phenethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;
- N-{3-[3-(4-Fluoro-benzyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;
- 35 N-{3-[3-(2-Ethyl-hexyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;

- N-[3-(8-Methoxy-3-octyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenyl]-methanesulfonamide;  
N-{3-[3-(2-Hydroxy-indan-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;  
N-{3-[3-(4-Chloro-benzyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;  
5 N-(3-{8-Hydroxy-3-[3-(1-hydroxy-cyclohexyl)-propyl]-3-aza-bicyclo[3.2.1]oct-8-yl}-phenyl)-methanesulfonamide;  
N-{3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;  
10 N-{3-[8-Hydroxy-3-(2-hydroxy-indan-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;  
N-(3-{3-[3-(1-Hydroxy-cyclohexyl)-propyl]-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl}-phenyl)-methanesulfonamide;  
N-{3-[8-Hydroxy-3-(2-hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;  
15 N-{3-[3-(2-Hydroxy-indan-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;  
N-{3-[3-(2-Hydroxy-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl)-8-methoxy-3-aza-bicyclo[3.2.1]oct-8-yl]-phenyl}-methanesulfonamide;  
20 3-(3-Cyclopropylmethyl-3-aza-bicyclo[3.2.1]oct-8-yl)-phenol;  
3-(3-Cyclopropylmethyl-8-hydroxy-3-aza-bicyclo[3.2.1]oct-8-yl)-phenol;  
3-{3-[3-(1-Hydroxy-cyclohexyl)-propyl]-3-aza-bicyclo[3.2.1]oct-8-yl}-phenol;  
3-[3-(1-Hydroxy-cyclohexyl)-propyl]-8-(3-hydroxy-phenyl)-3-aza-bicyclo[3.2.1]octan-8-ol;  
25 3-[3-(3-Cyclohexyl-propyl)-3-aza-bicyclo[3.2.1]oct-8-yl]-phenol;  
3-(3-Cyclohexyl-propyl)-8-(3-hydroxy-phenyl)-3-aza-bicyclo[3.2.1]octan-8-ol;  
2-[8-(3-Hydroxy-phenyl)-3-aza-bicyclo[3.2.1]oct-3-ylmethyl]-indan-2-ol; and  
3-(2-Hydroxy-indan-2-ylmethyl)-8-(3-hydroxy-phenyl)-3-aza-bicyclo[3.2.1]octan-8-ol;  
and pharmaceutically acceptable salts thereof.
- 30 11. A pharmaceutical composition comprising an effective amount of a compound according to claim 1 in combination with a pharmaceutically acceptable carrier, excipient or additive.
12. A method of treating in a mammal, in need thereof, a disease state, disorder or condition selected from the group consisting of irritable bowel syndrome, constipation,  
35 nausea, vomiting, pruritic dermatoses, psoriasis; eczema; an insect bite; eating disorders, depression, anxiety, schizophrenia; drug addiction, an opioid overdose, sexual dysfunction, stroke, head trauma, traumatic brain injury, spinal damage, Parkinson's disease, Alzheimer's

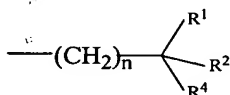
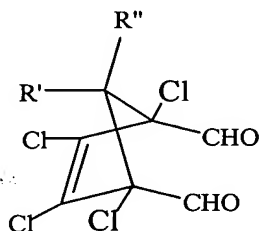
disease, age-related cognitive decline and Attention Deficit and Hyperactivity Disorder, said method comprising administering to said mammal an amount of a compound according to claim 1 effective in treating said disease state, disorder or condition.

13. A method of synthesizing a compound of the formula:



5

comprising reacting a primary amine compound of formula  $R^aNH_2$  with a compound of the formula:



10

where  $R^a$  is H or a

group;

15

$R^1$  and  $R^2$  are independently H, a  $C_1$ - $C_6$  alkyl,  $-(CH_2)_j$ -aryl,  $-(CH_2)_j$ -heteroaryl, wherein said alkyl,  $-(CH_2)_j$ -aryl or  $-(CH_2)_j$ -heteroaryl group is optionally substituted with one or more  $R^{16}$  groups, or with the carbon to which  $R^1$  and  $R^2$  are attached,  $R^1$  and  $R^2$  form a  $C_3$ - $C_7$  carbocyclic or 4- to 7-membered heterocyclic group, wherein said heterocyclic group comprises from one to three heteroatoms selected from the group consisting of O, S and N and said carbocyclic or heterocyclic group optionally contains a  $-C(=O)$  group or optionally contains one or more double bonds and is optionally fused to or substituted with a  $C_6$ - $C_{14}$  aryl or a 5- to 14-membered heteroaryl group, wherein said  $C_3$ - $C_7$  carbocyclic or 4- to 7-membered heterocyclic group formed by  $R^1$  and  $R^2$  may optionally be substituted with from one to three  $R^{16}$  groups, and said optionally fused or substituted aryl or heteroaryl group may each optionally independently be substituted with from one to six  $R^{16}$  groups;

20

$R^4$  is absent or is H,  $-C_1$ - $C_4$  alkyl, which optionally contains one or two unsaturated bonds,  $-OH$ ,  $-O(C_1-C_4)alkyl$ ,  $-(C_1-C_4)alkylOH$ ,  $-(CH_2)_n-NR^{16a}R^{16b}$ ,  $-(CH_2)_n-NHC(=O)(C_1-C_4 alkyl)$ ,  $-(CH_2)_n-NO_2$ ,  $-(CH_2)_n-C\equiv N$ ,  $-(CH_2)_n-C(=O)NH_2$ ,  $-(CH_2)_n-C(=O)NR^{16a}R^{16b}$ ;

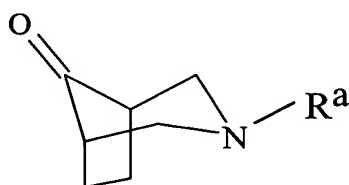


each  $R^{16a}$  and  $R^{16b}$  is independently selected from H and C<sub>1</sub>-C<sub>4</sub> alkyl; or, independently in each instance of  $-C(R^4)R^{16a}R^{16b}$ ,  $R^{16a}$  and  $R^{16b}$  connect to form a C<sub>3</sub>-C<sub>7</sub> carbocyclic ring;

j is in each instance independently an integer from 0 to 5;

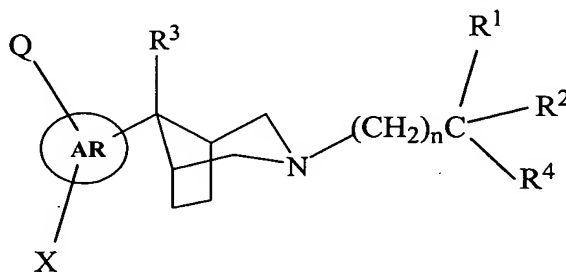
5 n is in each instance independently an integer from 0 to 5;

and R' and R'' together represent a carbonyl protecting group or groups, under reductive amination or reducing conditions; and thereafter removing said protecting groups R' and R'' to form



10

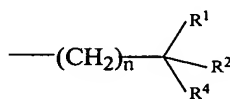
14. A method of synthesizing a compound of the formula IV:



IV

15

wherein R<sup>a</sup> is H or a



group;



is an aryl or heteroaryl group;

X is H, halogen, -OH, -CN,  $-C\equiv C-R^{3a}$ , a C<sub>1</sub>-C<sub>4</sub> alkyl group optionally substituted with from one to three halogen atoms, or a -O(C<sub>1</sub>-C<sub>4</sub> alkyl) group optionally substituted with from one to three halogen atoms;

20

Q is H, halogen, a C<sub>1</sub>-C<sub>6</sub> alkyl, -OH, -CN, -OCH<sub>3</sub>, -NH<sub>2</sub>, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)NH<sub>2</sub>, -C(=O)NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -NHC(=O)R<sup>15</sup>, -NHS(=O)<sub>2</sub>R<sup>15</sup>, a 5- to 7-membered carbocyclic or heterocyclic group, or forms

a 5- to 7-membered phenyl-fused or heteroaryl-fused carbocyclic or heterocyclic group with an adjacent atom on the phenyl or heteroaryl group to which it is attached, said phenyl-fused or heteroaryl-fused carbocyclic or heterocyclic group optionally containing at least one unsaturated bond, said heterocyclic group or said phenyl-fused or heteroaryl-fused heterocyclic group containing at least one heteroatom selected from nitrogen, oxygen and sulfur, said carbocyclic or heterocyclic group or said phenyl- or heteroaryl-fused carbocyclic or heterocyclic group being optionally substituted with at least one substituent selected from H, halogen, -OH, =O, -C≡C-R<sup>3a</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl, -O(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, or -(CH<sub>2</sub>)<sub>n</sub>-aryl, wherein said C<sub>1</sub>-C<sub>6</sub> alkyl, -O(C<sub>1</sub>-C<sub>6</sub>)alkyl, or C<sub>3</sub>-C<sub>6</sub> cycloalkyl groups optionally may be substituted by one or more halogen atoms and said aryl portion of said -(CH<sub>2</sub>)<sub>n</sub>-aryl is optionally substituted by one or more substituents selected from H, halogen, C<sub>1</sub>-C<sub>4</sub> alkyl and -O(C<sub>1</sub>-C<sub>4</sub>)alkyl, said C<sub>1</sub>-C<sub>4</sub> alkyl and -O(C<sub>1</sub>-C<sub>4</sub>)alkyl groups being optionally substituted by one or more halogen atoms, -N(R<sup>4a</sup>)(R<sup>5a</sup>), -N(R<sup>4b</sup>)S(O)<sub>m</sub>R<sup>6a</sup>, -N(R<sup>4c</sup>)C(O)R<sup>7a</sup> or -N(R<sup>4d</sup>)C(O)OR<sup>7b</sup> groups;

R<sup>3a</sup>, R<sup>4a</sup>, R<sup>4b</sup>, R<sup>4c</sup>, R<sup>4d</sup> and R<sup>5a</sup> are independently H or C<sub>1</sub>-C<sub>6</sub> alkyl which may be optionally substituted with one or more halogen groups, or R<sup>4a</sup> and R<sup>5a</sup>, together with the nitrogen atom to which they are bound, form a 4- to 7-membered heterocyclic group which may be unsubstituted or substituted with one or more substituents selected from C<sub>1</sub>-C<sub>4</sub> alkyl, -O(C<sub>1</sub>-C<sub>4</sub>)alkyl, -OH, =O, -NR<sup>16a</sup>R<sup>16b</sup>, halogen or -C≡C-R<sup>3a</sup>;

R<sup>6a</sup> is a C<sub>1</sub>-C<sub>6</sub> alkyl, an aryl or a heteroaryl group wherein said alkyl, aryl or heteroaryl group is unsubstituted or substituted with one or more substituents selected from halogen, C<sub>1</sub>-C<sub>4</sub> alkyl, -OH, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), -(C<sub>1</sub>-C<sub>4</sub> alkyl)-O-(C<sub>1</sub>-C<sub>4</sub> alkyl) or -(CH<sub>2</sub>)<sub>n</sub>-NR<sup>21</sup>R<sup>22</sup>;

R<sup>7a</sup> and R<sup>7b</sup> are independently selected from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl (wherein each of said C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl may independently be unsubstituted or substituted with halogen or C<sub>1</sub>-C<sub>4</sub> alkyl substituents), or R<sup>7a</sup> is H;

R<sup>1</sup> and R<sup>2</sup> are independently H, a C<sub>1</sub>-C<sub>6</sub> alkyl, -(CH<sub>2</sub>)<sub>j</sub>-aryl, -(CH<sub>2</sub>)<sub>j</sub>-heteroaryl, wherein said alkyl, -(CH<sub>2</sub>)<sub>j</sub>-aryl or -(CH<sub>2</sub>)<sub>j</sub>-heteroaryl group is optionally substituted with one or more R<sup>16</sup> groups, or with the carbon to which R<sup>1</sup> and R<sup>2</sup> are attached, R<sup>1</sup> and R<sup>2</sup> form a C<sub>3</sub>-C<sub>7</sub> carbocyclic or 4- to 7-membered heterocyclic group, wherein said heterocyclic group comprises from one to three heteroatoms selected from the group consisting of O, S and N and said carbocyclic or heterocyclic group optionally contains a -C(=O) group or optionally contains one or more double bonds and is optionally fused to or substituted with a C<sub>6</sub>-C<sub>14</sub> aryl or a 5- to 14-membered heteroaryl group, wherein said C<sub>3</sub>-C<sub>7</sub> carbocyclic or 4- to 7-membered heterocyclic group formed by R<sup>1</sup> and R<sup>2</sup> may optionally be substituted with from one to three R<sup>16</sup> groups, and said optionally fused or substituted aryl or heteroaryl group may each optionally independently be substituted with from one to six R<sup>16</sup> groups;

each  $R^{16}$  is independently selected from  $R^{17}$ , H, halogen,  $-OR^{17}$ ,  $-NO_2$ ,  $-CN$ ,  $-C_1-C_6$  alkyl,  $-C_3-C_6$  cycloalkyl,  $-C(R^4)R^{16a}R^{16b}$ , aryl optionally substituted with from 1 to 3  $R^4$  groups,  $-(CH_2)_vNR^{17}R^{18}$ ,  $-NR^{17}C(=O)R^{18}$ ,  $-C(=O)NR^{17}R^{18}$ ,  $-OC(=O)R^{17}$ ,  $-C(=O)OR^{17}$ ,  $-C(=O)R^{17}$ ,  $-NR^{17}C(=O)OR^{18}$ ,  $-NR^{17}C(=O)NR^{18}R^{19}$ ,  $-NR^{17}S(=O)_2R^{18}$ ,  $-NR^{17}S(=O)_2NR^{18}R^{19}$ , and  $-S(=O)_2R^{17}$ ;

$R^3$  is H, F, Cl,  $-OH$ ,  $-C_1-C_4$  alkyl,  $-C\equiv N$ ,  $-NR^{17}C(=O)R^{18}$ ,  $-C(=O)NR^{17}R^{18}$ ,  $-O(C_1-C_4)alkyl$ ,  $-(CH_2)_nOH$ ,  $-(CH_2)_n-C\equiv N$ ,  $-(CH_2)_n-NR^{17}C(=O)R^{18}$ ,  $-(CH_2)_n-C(=O)NR^{17}R^{18}$ ,  $-(CH_2)_n-O(C_1-C_4)alkyl$ , or  $-(CH_2)_n-NR^{16a}R^{16b}$ ;

$R^4$  is absent or is H,  $-C_1-C_4$  alkyl, which optionally contains one or two unsaturated bonds,  $-OH$ ,  $-O(C_1-C_4)alkyl$ ,  $-(C_1-C_4)alkylOH$ ,  $-(CH_2)_n-NR^{16a}R^{16b}$ ,  $-(CH_2)_n-NHC(=O)(C_1-C_4)alkyl$ ,  $-(CH_2)_n-NO_2$ ,  $-(CH_2)_n-C\equiv N$ ,  $-(CH_2)_n-C(=O)NH_2$ ,  $-(CH_2)_n-C(=O)NR^{16a}R^{16b}$ ;

$R^{15}$ ,  $R^{17}$ ,  $R^{18}$  and  $R^{19}$  are independently H,  $-C_1-C_4$  alkyl,  $-(C_2-C_4)alkyl-O-(C_1-C_4)alkyl$ ,  $-(CH_2)_v-NR^{21}R^{22}$ , or a 4- to 7-membered heterocyclic group optionally substituted with a  $-C_1-C_4$  alkyl;

each  $R^{16a}$  and  $R^{16b}$  is independently selected from H and  $C_1-C_4$  alkyl; or, independently in each instance of  $-C(R^4)R^{16a}R^{16b}$ ,  $R^{16a}$  and  $R^{16b}$  connect to form a  $C_3-C_7$  carbocyclic ring;

$R^{20}$  is a  $C_1-C_4$  alkyl group, a  $C_3-C_7$  carbocyclic or a 4- to 7-membered heterocyclic group comprising from one to three heteroatoms selected from the group consisting of O, S and N, wherein said carbocyclic and heterocyclic groups are optionally independently substituted with from one to three  $R^{16}$  groups, optionally independently contain one or more double bonds, and are optionally fused to a  $C_6-C_{14}$  aryl or a  $C_5-C_{14}$  heteroaryl group comprising from one to three heteroatoms selected from the group consisting of O, S and N, and wherein said optionally fused aryl or heteroaryl groups can each optionally independently be substituted with from one to six  $R^{16}$  groups;

$R^{21}$  and  $R^{22}$  are each independently H or  $C_1-C_6$  alkyl; or, independently in each instance of  $-NR^{21}R^{22}$ ,  $R^{21}$  and  $R^{22}$  connect to form a 4- to 7-membered heterocyclic ring comprising from one to three heteroatoms selected from O, S, and N;

j is in each instance independently an integer from 0 to 5;

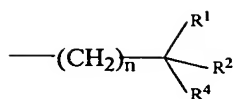
m is in each instance independently an integer from 0 to 2;

n is in each instance independently an integer from 0 to 5;

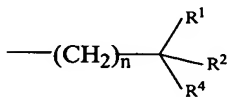
v is in each instance independently an integer from 0 to 5;

or a pharmaceutically acceptable salt thereof;

with the provisos that

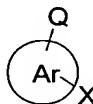


a) when  $R^a$  is and  $n$  is 0, and when the carbon to which  $R^1$ ,  $R^2$  and  $R^4$  are bound is  $sp^3$  hybridized (i.e., "saturated"), then none of  $R^1$ ,  $R^2$  and  $R^4$  can be a heteroatom or contain a heteroatom which is directly linked to the carbon of said



group;

- 5 b)  $R^{15}$  cannot be H when part of a  $-NHS(=O)_2R^{15}$  group,  $R^{17}$  cannot be H when part of a  $-S(=O)_2R^{17}$  group and  $R^{18}$  cannot be H when part of a  $-NR^{17}S(=O)_2R^{18}$  group;

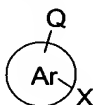


c) when  $R^3$  is  $OCH_3$  or  $OH$ , cannot be 3-hydroxyphenyl or 3-methoxyphenyl;



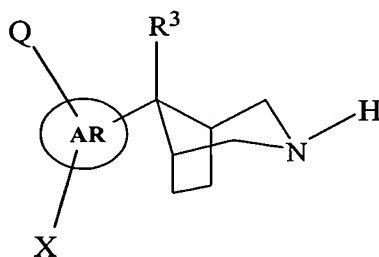
d) when is a phenyl group, then  $Q$  and  $X$  are not both H;

e) when  $-(CH_2)_v-$  is connected to N, O, or S, then  $v$  cannot be 1; and

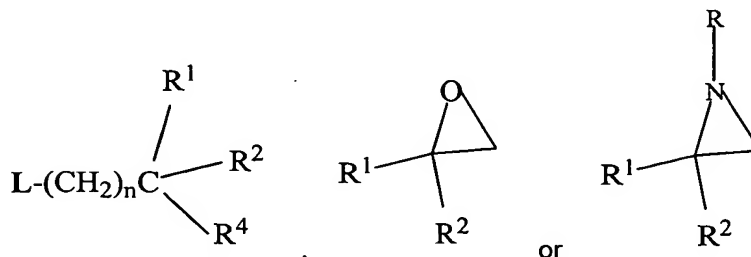


- 10 f) cannot be 4-(6-amino-pyridin-2-yl)-phenyl;

which method comprises reacting a compound according to the chemical structure:

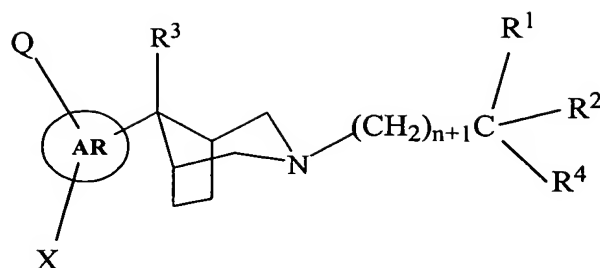


with a reactive compound according to the chemical structure:

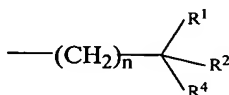


- 15 where  $L$  is a leaving group,  $R$  is H,  $SO_2R^b$  or  $CO_2R^b$  and  $R^b$  is an aryl or a  $C_1$ - $C_4$  alkyl group to provide a compound of the formula IV.

15. A method of synthesizing a compound according to chemical structure IVa:



IVa



5 wherein R<sup>a</sup> is H or a



is an aryl or heteroaryl group;

X is H, halogen, -OH, -CN, -C≡C-R<sup>3a</sup>, a -C<sub>1</sub>-C<sub>4</sub> alkyl group optionally substituted with from one to three halogen atoms, or a -O(C<sub>1</sub>-C<sub>4</sub> alkyl) group optionally substituted with from one to three halogen atoms;

10 Q is H, halogen, a C<sub>1</sub>-C<sub>6</sub> alkyl, -OH, -CN, -OCH<sub>3</sub>, -NH<sub>2</sub>, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)NH<sub>2</sub>, -C(=O)NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -NHC(=O)R<sup>15</sup>, -NHS(=O)<sub>2</sub>R<sup>15</sup>, a 5- to 7-membered carbocyclic or heterocyclic group, or forms  
15 heteroaryl-fused carbocyclic or heterocyclic group optionally containing at least one unsaturated bond, said heterocyclic group or said phenyl-fused or heteroaryl-fused heterocyclic group containing at least one heteroatom selected from nitrogen, oxygen and sulfur, said carbocyclic or heterocyclic group or said phenyl- or heteroaryl-fused carbocyclic or heterocyclic group being optionally substituted with at least one substituent selected from H,  
20 halogen, -OH, =O, -C≡C-R<sup>3a</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl, -O(C<sub>1</sub>-C<sub>6</sub>)alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, or -(CH<sub>2</sub>)<sub>n</sub>-aryl, wherein said C<sub>1</sub>-C<sub>6</sub> alkyl, -O(C<sub>1</sub>-C<sub>6</sub>)alkyl, or C<sub>3</sub>-C<sub>6</sub> cycloalkyl groups optionally may be substituted by one or more halogen atoms and said aryl portion of said -(CH<sub>2</sub>)<sub>n</sub>-aryl is optionally substituted by one or more substituents selected from H, halogen, C<sub>1</sub>-C<sub>4</sub> alkyl and -O(C<sub>1</sub>-C<sub>4</sub>)alkyl, said C<sub>1</sub>-C<sub>4</sub> alkyl and -O(C<sub>1</sub>-C<sub>4</sub>)alkyl groups being optionally substituted by one  
25 or more halogen atoms, -N(R<sup>4a</sup>)(R<sup>5a</sup>), -N(R<sup>4b</sup>)S(O)<sub>m</sub>R<sup>6a</sup>, -N(R<sup>4c</sup>)C(O)R<sup>7a</sup> or -N(R<sup>4d</sup>)C(O)OR<sup>7b</sup> groups;

R<sup>3a</sup>, R<sup>4a</sup>, R<sup>4b</sup>, R<sup>4c</sup>, R<sup>4d</sup> and R<sup>5a</sup> are independently H or C<sub>1</sub>-C<sub>6</sub> alkyl which may be optionally substituted with one or more halogen groups, or R<sup>4a</sup> and R<sup>5a</sup>, together with the

nitrogen atom to which they are bound, form a 4- to 7-membered heterocyclic group which may be unsubstituted or substituted with one or more substituents selected from C<sub>1</sub>-C<sub>4</sub> alkyl, -O(C<sub>1</sub>-C<sub>4</sub>)alkyl, -OH, =O, -NR<sup>16a</sup>R<sup>16b</sup>, halogen or -C≡C-R<sup>3a</sup>;

R<sup>6a</sup> is a C<sub>1</sub>-C<sub>6</sub> alkyl, an aryl or a heteroaryl group wherein said alkyl, aryl or heteroaryl group is unsubstituted or substituted with one or more substituents selected from halogen, C<sub>1</sub>-C<sub>4</sub> alkyl, -OH, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), -(C<sub>1</sub>-C<sub>4</sub> alkyl)-O-(C<sub>1</sub>-C<sub>4</sub> alkyl) or -(CH<sub>2</sub>)<sub>n</sub>-NR<sup>21</sup>R<sup>22</sup>;

R<sup>7a</sup> and R<sup>7b</sup> are independently selected from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl (wherein each of said C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl may independently be unsubstituted or substituted with halogen or C<sub>1</sub>-C<sub>4</sub> alkyl substituents), or R<sup>7a</sup> is H;

R<sup>1</sup> and R<sup>2</sup> are independently H, a C<sub>1</sub>-C<sub>6</sub> alkyl, -(CH<sub>2</sub>)<sub>j</sub>-aryl, -(CH<sub>2</sub>)<sub>j</sub>-heteroaryl, wherein said alkyl, -(CH<sub>2</sub>)<sub>j</sub>-aryl or -(CH<sub>2</sub>)<sub>j</sub>-heteroaryl group is optionally substituted with one or more R<sup>16</sup> groups, or with the carbon to which R<sup>1</sup> and R<sup>2</sup> are attached, R<sup>1</sup> and R<sup>2</sup> form a C<sub>3</sub>-C<sub>7</sub> carbocyclic or 4- to 7-membered heterocyclic group, wherein said heterocyclic group comprises from one to three heteroatoms selected from the group consisting of O, S and N and said carbocyclic or heterocyclic group optionally contains a -C(=O) group or optionally contains one or more double bonds and is optionally fused to or substituted with a C<sub>6</sub>-C<sub>14</sub> aryl or a 5- to 14-membered heteroaryl group, wherein said C<sub>3</sub>-C<sub>7</sub> carbocyclic or 4- to 7-membered heterocyclic group formed by R<sup>1</sup> and R<sup>2</sup> may optionally be substituted with from one to three R<sup>16</sup> groups, and said optionally fused or substituted aryl or heteroaryl group may each optionally independently be substituted with from one to six R<sup>16</sup> groups;

each R<sup>16</sup> is independently selected from R<sup>17</sup>, H, halogen, -OR<sup>17</sup>, -NO<sub>2</sub>, -CN, -C<sub>1</sub>-C<sub>6</sub> alkyl, -C<sub>3</sub>-C<sub>6</sub> cycloalkyl, -C(R<sup>4</sup>)R<sup>16a</sup>R<sup>16b</sup>, aryl optionally substituted with from 1 to 3 R<sup>4</sup> groups, -(CH<sub>2</sub>)<sub>v</sub>NR<sup>17</sup>R<sup>18</sup>, -NR<sup>17</sup>C(=O)R<sup>18</sup>, -C(=O)NR<sup>17</sup>R<sup>18</sup>, -OC(=O)R<sup>17</sup>, -C(=O)OR<sup>17</sup>, -C(=O)R<sup>17</sup>, -NR<sup>17</sup>C(=O)OR<sup>18</sup>, -NR<sup>17</sup>C(=O)N R<sup>18</sup>R<sup>19</sup>, -NR<sup>17</sup>S(=O)<sub>2</sub>R<sup>18</sup>, -NR<sup>17</sup>S(=O)<sub>2</sub>NR<sup>18</sup>R<sup>19</sup>, and -S(=O)<sub>2</sub>R<sup>17</sup>;

R<sup>3</sup> is H, F, Cl, -OH, -C<sub>1</sub>-C<sub>4</sub> alkyl, -C≡N, -NR<sup>17</sup>C(=O)R<sup>18</sup>, -C(=O)NR<sup>17</sup>R<sup>18</sup>, -O(C<sub>1</sub>-C<sub>4</sub>)alkyl, -(CH<sub>2</sub>)<sub>n</sub>OH, -(CH<sub>2</sub>)<sub>n</sub>-C≡N, -(CH<sub>2</sub>)<sub>n</sub>-NR<sup>17</sup>C(=O)R<sup>18</sup>, -(CH<sub>2</sub>)<sub>n</sub>-C(=O)NR<sup>17</sup>R<sup>18</sup>, -(CH<sub>2</sub>)<sub>n</sub>-O(C<sub>1</sub>-C<sub>4</sub>)alkyl, or -(CH<sub>2</sub>)<sub>n</sub>-NR<sup>16a</sup>R<sup>16b</sup>;

R<sup>4</sup> is absent or is H, -C<sub>1</sub>-C<sub>4</sub> alkyl, which optionally contains one or two unsaturated bonds, -OH, -O(C<sub>1</sub>-C<sub>4</sub>)alkyl, -(C<sub>1</sub>-C<sub>4</sub>)alkylOH, -(CH<sub>2</sub>)<sub>n</sub>-NR<sup>16a</sup>R<sup>16b</sup>, -(CH<sub>2</sub>)<sub>n</sub>-NHC(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -(CH<sub>2</sub>)<sub>n</sub>-NO<sub>2</sub>, -(CH<sub>2</sub>)<sub>n</sub>-C≡N, -(CH<sub>2</sub>)<sub>n</sub>-C(=O)NH<sub>2</sub>, -(CH<sub>2</sub>)<sub>n</sub>-C(=O)NR<sup>16a</sup>R<sup>16b</sup>;

R<sup>15</sup>, R<sup>17</sup>, R<sup>18</sup> and R<sup>19</sup> are independently H, -C<sub>1</sub>-C<sub>4</sub> alkyl, -(C<sub>2</sub>-C<sub>4</sub> alkyl)-O-(C<sub>1</sub>-C<sub>4</sub> alkyl), -(CH<sub>2</sub>)<sub>v</sub>-NR<sup>21</sup>R<sup>22</sup>, or a 4- to 7-membered heterocyclic group optionally substituted with a -C<sub>1</sub>-C<sub>4</sub> alkyl;

each R<sup>16a</sup> and R<sup>16b</sup> is independently selected from H and C<sub>1</sub>-C<sub>4</sub> alkyl; or, independently in each instance of -C(R<sup>4</sup>)R<sup>16a</sup>R<sup>16b</sup>, R<sup>16a</sup> and R<sup>16b</sup> connect to form a C<sub>3</sub>-C<sub>7</sub> carbocyclic ring;

$R^{20}$  is a  $C_1$ - $C_4$  alkyl group, a  $C_3$ - $C_7$  carbocyclic or a 4- to 7-membered heterocyclic group comprising from one to three heteroatoms selected from the group consisting of O, S and N, wherein said carbocyclic and heterocyclic groups are optionally independently substituted with from one to three  $R^{16}$  groups, optionally independently contain one or more  
 5 double bonds, and are optionally fused to a  $C_6$ - $C_{14}$  aryl or a  $C_5$ - $C_{14}$  heteroaryl group comprising from one to three heteroatoms selected from the group consisting of O, S and N, and wherein said optionally fused aryl or heteroaryl groups can each optionally independently be substituted with from one to six  $R^{16}$  groups;

$R^{21}$  and  $R^{22}$  are each independently H or  $C_1$ - $C_6$  alkyl; or, independently in each  
 10 instance of  $-NR^{21}R^{22}$ ,  $R^{21}$  and  $R^{22}$  connect to form a 4- to 7-membered heterocyclic ring comprising from one to three hetero atoms selected from O, S, and N;

j is in each instance independently an integer from 0 to 5;

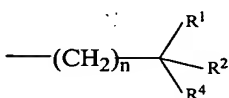
m is in each instance independently an integer from 0 to 2;

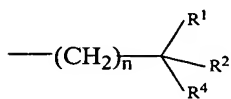
n is in each instance independently an integer from 0 to 5;

15 v is in each instance independently an integer from 0 to 5;

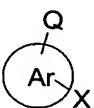
or a pharmaceutically acceptable salt thereof;


with the provisos that

a) when  $R^a$  is  and n is 0, and when the carbon to which  $R^1$ ,  $R^2$  and  $R^4$  are bound is  $sp^3$  hybridized (i.e., "saturated"), then none of  $R^1$ ,  $R^2$  and  $R^4$  can be a  
 20 heteroatom or contain a heteroatom which is directly linked to the carbon of said

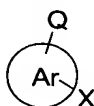
 group;

b)  $R^{15}$  cannot be H when part of a  $-NHS(=O)_2R^{15}$  group,  $R^{17}$  cannot be H when part of a  $-S(=O)_2R^{17}$  group and  $R^{18}$  cannot be H when part of a  $-NR^{17}S(=O)_2R^{18}$  group;

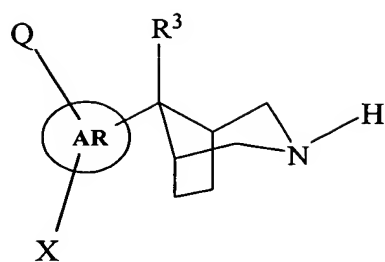
c) when  $R^3$  is  $OCH_3$  or OH,  cannot be 3-hydroxyphenyl or 3-methoxyphenyl;

d) when  is a phenyl group, then Q and X are not both H;

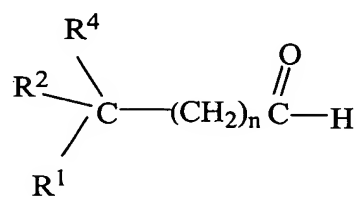
e) when  $-(CH_2)_v-$  is connected to N, O, or S, then v cannot be 1; and

f)  cannot be 4-(6-amino-pyridin-2-yl)-phenyl;

which method comprises reacting a compound according to the chemical structure:



with a compound according to the structure:



under reductive amination or reducing conditions to produce the compound of formula

5 IVa.